

# Solid oral forms availability in children: a cost saving investigation

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## WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Oral liquid drug formulations, historically considered as the most appropriate medicine for paediatric patients, present numerous disadvantages (low stability, inappropriate excipients).
- Solid forms are more convenient, less costly and improve drug compliance in children.
- Pill swallowing training significantly improves the ability to swallow orally administered solids from the age of 3 years old.

## WHAT THIS STUDY ADDS

- Considering dosage acceptability of solid forms, approximately 80% of prescribed liquid formulations could be substituted with a solid form in children aged over 2 years.
- Considering both dosage and size suitability, half of liquid drugs could be substituted, tablet size being the major limitation for solid form use in children.
- From both hospital and community perspectives, three quarters of treatment costs may be saved for liquid formulations that could be substituted.

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## Keywords

drug formulation, oral drug delivery,  
paediatric, swallowing

## Received

13 February 2014

## Accepted

7 June 2014

## Accepted Article Published Online

25 June 2014

## AIM

To assess the suitability and potential cost savings, from both the hospital and community perspective, of prescribed oral liquid medicine substitution with acceptable solid forms for children over 2 years.

## METHOD

Oral liquid medicines dispensed from a paediatric hospital (UK) in 1 week were assessed by screening for existence of the solid form alternative and evaluating the acceptability of the available solid form, firstly related to the prescribed dose and secondly to acceptable size depending on the child's age. Costs were calculated based on providing treatment for 28 days or prescribed duration for short term treatments.

## RESULTS

Over 90% (440/476) of liquid formulations were available as a marketed solid form. Considering dosage acceptability (maximum of 10% deviation from prescribed dosage or 0% for narrow therapeutic range drugs, maximum tablet divisions into quarters) 80% of liquids could be substituted with a solid form. The main limitation for liquid substitution would be solid form size. However, two-thirds of prescribed liquids could have been substituted with a suitable solid form for dosage and size, with estimated savings being of £5K and £8K in 1 week, respectively based on hospital and community costs, corresponding to a projected annual saving of £238K and £410K (single institution).

## CONCLUSION

Whilst not all children over 2 years will be able to swallow tablets, drug cost savings if oral liquid formulations were substituted with suitable solid dosage forms would be considerable. Given the numerous advantages of solid forms compared with liquids, this study may provide a theoretical basis for investing in supporting children to swallow tablets/capsules.

## Introduction

Since the adoption of the Paediatric Regulation (EC) no. 1901/2006 and the emergence of expert committees in paediatric medicine, a significant part of research in paediatric pharmacology is now focused on drug formulation, fundamentally determining whether the dose of the active pharmaceutical ingredient can be successfully delivered to children [1–4]. The availability of an appropriate drug form is of major concern for paediatricians, nurses, pharmacists and parents. Paediatric medicines have to be safe, well tolerated, easy to use (palatable and requiring minimal manipulations), transportable, easily produced, cost effective and commercially viable and have a minimal impact on life-style [1, 4]. Oral liquid drug formulations, including solutions, syrups, suspensions and emulsions, are considered as the most appropriate oral formulation for children, since they are developed for younger infants unable to swallow tablets or capsules and accommodate palatability changes required by children [1, 5, 6]. However, liquid formulations present numerous disadvantages, such as low stability, difficulties in taste masking, inappropriate excipients for children (e.g. propylene glycol, benzyl alcohol, sweeteners for diabetics) and low transportability [1, 2, 7]. In the long term, dose volume and frequency of administration can lead to reduced compliance in children receiving multiple drugs [8]. In addition, liquid drugs for children are often provided as unlicensed medicines, when no licensed suitable alternative is available. Unlicensed medicines are often much more expensive than licensed products. Finally, oral liquid medicine multiple preparation steps, such as suspension reconstitution and homogenization, dose and volume calculation and precision of volume measurement [9], as well as misunderstanding of instruction for liquid medicines use by caregivers [10, 11], are risk factors for medicine error in children [12]. Most administration errors in children result from decimal place errors or confusion between mg and ml [11, 13].

An alternative to liquid formulations is the conventional solid oral dosage form, such as tablets or capsules. These offer the advantages of greater stability, easy dose selection, improved transportability and ease of storage [2, 14]. Solid forms also allow the modification of drug pharmacokinetic parameters, minimizing administration frequency and indirectly improving drug compliance [1, 15, 16]. Oral solid forms are much less costly than liquid formulations, since they are easier to develop, manufacture, transport, store and dispense. However, despite those significant advantages and the recent change of paradigm in solid dosage form acceptability in children from numerous experts in paediatric pharmacology [1, 2, 4, 8], there is a lack of evidence concerning solid dosage form acceptability in children and in particular their ability to swallow tablets or capsules. Solid dosage forms remain unpopular in paediatric practice. The primary explanation

would be the assumed inability for children to swallow whole the solid form safely, avoiding risks of inhalation and choking. Nevertheless, some published studies have shown that solid forms can be swallowed by very young children, including children as young as 6 months of age [4, 8, 17–19]. Another limitation which may also explain the low use of oral solid forms in paediatrics is the lack of dosing flexibility compared with liquid formulations without crushing tablets [2, 20]. Indeed, an important practical issue in paediatrics is to ensure that the chosen formulation can provide an accurate and appropriate dose for the children's needs. To date there are no published studies which have evaluated the concordance between the marketed dosages of oral solid forms and the prescribed doses in paediatrics.

Considering these two assumed limitations for the use of solid forms in children, the objective of this study was to assess the availability and the suitability of solid oral dosage forms for prescribed liquid medicines in children over 2 years of age. Considering that crushing tablets carries risks of preparation error, loss of stability and administration complexities this study has been conducted based on the assumption that tablets have to be swallowed by children, whole, halved or quartered. Results allow estimating the potential cost savings that could be made to the NHS (based on both hospital and community pharmacy prices) if all children over 2 years were converted from liquid to solid formulations where there is an available and acceptable solid form. This cost estimate supports answering the research question asked by the Expert Committee on Selection and Use of Essential Medicines (WHO committee) about dosage forms of medicines for children: 'What are true component costs of different dosage forms of medicines for children?' [6].

## Methods

### *Data sources*

A cross-sectional single site study was performed on anonymized pharmacy records of dispensed medicines in Birmingham Children's Hospital (BCH) for patients of 2 years old and above during 1 week (7–13th January 2013). Data were extracted from the BCH dispensing software database (Ascribe®, ASC, Bolton, UK). For each dispensed item the following information was recorded: child's age, drug international non-proprietary and commercial names, unit and daily prescribed dosage, dispensed pharmaceutical dosage form, treatment duration, quantity dispensed and cost of total drug quantity delivered from hospital prices.

Approval for this observational study was obtained from the National Research Ethics Service (Manchester, UK).

### *Suitability of oral solid forms*

Substitution suitability with oral solid dosage form for each dispensed liquid medicine was determined:

- 1 Firstly by screening for the existence of the prescribed oral liquid drug in a marketed solid form alternative. The existence of an alternative marketed oral solid form was assessed consulting Ascribe® and the electronic Medicines Compendium (eMC) website.
- 2 Secondly by evaluating the suitability of available solid form dosage(s) related to the prescribed dose. Solid dosage concordance with prescribed dose was assessed for each dispensed liquid formulation existing as a marketed solid form. The maximum tablet division considered acceptable for appropriately scored tablets was the quarter (coated and time-released tablets were excluded from splitting). We considered that solid forms have to be swallowed (whole, halved or quartered) and not crushed. If, in spite of tablet division, the prescribed dose and available solid form dosage(s) did not fully match, the possibility of rounding the prescribed dose was evaluated by a hospital pharmacist considering the drug therapeutic index, current indication and the recommended dosage in the British National Formulary (BNF) for Children 2012–2013 regarding the child's age. The maximum recommended dose should not be exceeded and the maximum accepted dose deviation from the prescribed dose was 10% with a dosing error being defined as any dose deviation of more than 10% [21, 22]. No dose adjustment was envisaged for narrow therapeutic index drugs, such as immunosuppressive medicines (e.g. azathioprine, ciclosporin, tacrolimus), anti-epileptics (e.g. carbamazepine, gabapentin, phenytoin, sodium valproate) or anticoagulants (e.g. warfarin).
- 3 Lastly by evaluating the solid size suitability depending on the child's age. The size suitability for solid forms available in an acceptable dosage, exactly or after dose rounding, was determined considering the guideline on pharmaceutical development of medicines for paediatric use of the Committee for Medicinal Products for Human Use (CHMP, European Medicines Agency's committee) of 2011 [23]: 3–5 mm diameter tablets are acceptable above 2 years of age, 5–10 mm diameter tablets are acceptable above 6 years, 10–15 mm diameter tablets are acceptable above 12 years and larger than 15 mm diameter tablets are not acceptable for the entire paediatric population, below 18 years. Despite solid form size suitability guidance having now been removed from the CHMP's draft update (2013) [3], no equivalent recommendation or opinion from any referral paediatric committee has been proposed since. Given the lack of published evidence for solid form size acceptability in children, we considered the CHMP's 2011 guidance to be the most authoritative publication to indicate solid size suitability depending on the child's age. The size of the

tablets in mm for available marketed solid forms was obtained from TICTAC® software, a toxicology software referencing the diameter of marketed drugs in UK (London, UK).

### *Cost estimates*

Hospital prices of dispensed liquid medicines during the study period were obtained from Ascribe® software, which holds the hospital prices applicable to the study institution. Cost of treatment with suitable solid forms was calculated by determining the equivalent number of doses required and the price of the unit dosage in Ascribe®. If tablet division was needed, we considered the cost of the section, assuming that all tablet sections were administered. For community prices the same process was implemented using the Drug Tariff published at the time of major hospital contract changes (November 2012, National Health Service Drug Tariff for England and Wales).

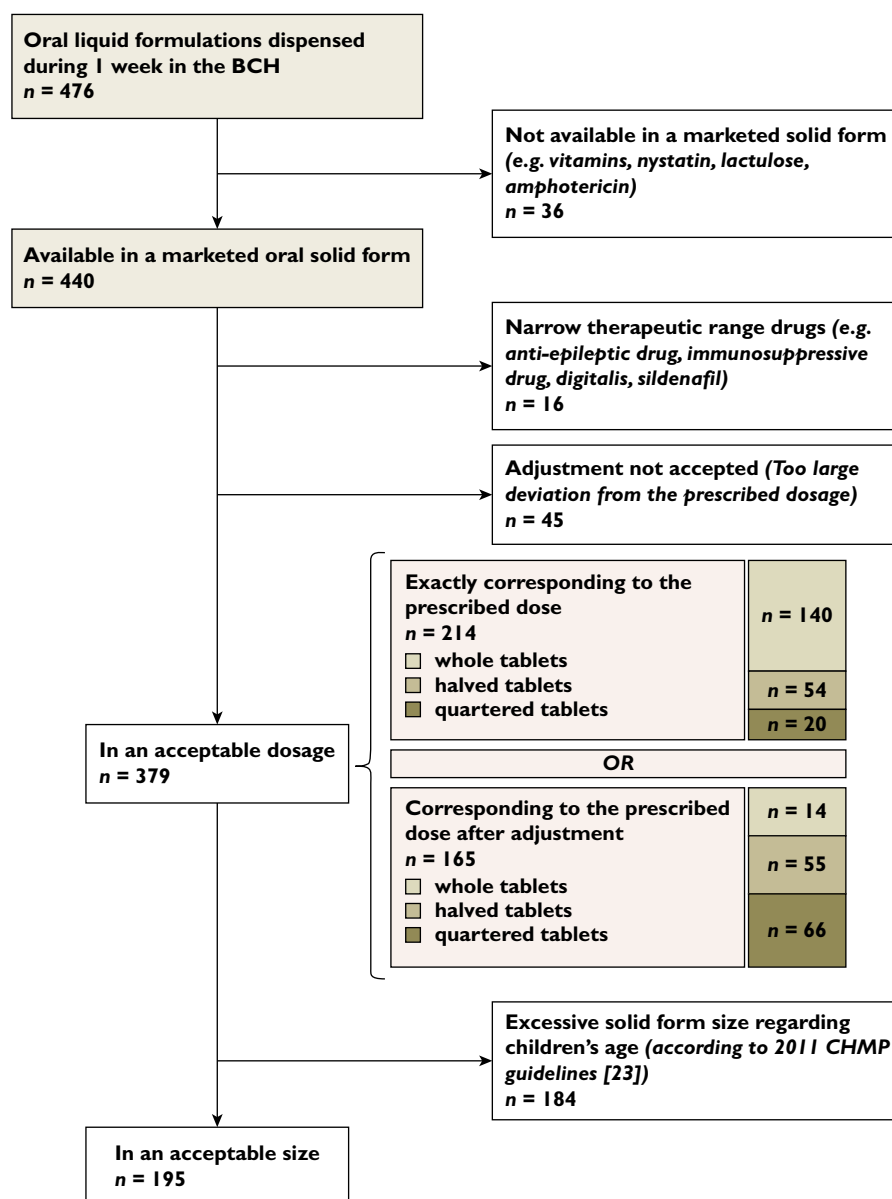
Calculated cost differences for each sector corresponded to the 'treatment cost of liquid formulations available in an acceptable solid form' minus the 'treatment cost of corresponding oral solid dosage forms' for the same dosage and treatment duration. The sum of these cost differences provides an estimate of the potential cost benefits if oral liquid drugs dispensed during the study period and having an acceptable solid form were substituted.

## **Results**

### *Suitability of oral solid forms*

Among the 908 dispensed oral medicine items for children over 2 years during 1 week by the BCH pharmacy (7–13th January 2013), 476 were prescribed as liquids. The mean age of children receiving oral liquid formulation was  $7.4 \pm 4.2$  years. The 10 most frequently prescribed liquid formulations were paracetamol (11%), ibuprofen (11%), codeine (10%), amoxicillin/clavulanic acid (5%), colecalciferol (5%), lactulose (3%), phenoxymethylpenicillin (2%), ondansetron (1%), ranitidine (1%) and omeprazole (1%). Of the dispensed liquid formulations 13% ( $n = 61$ ) were unlicensed medicines in the UK at the time of data collection.

Suitability of prescribed oral liquid medicine substitution with acceptable solid oral forms is detailed in Figure 1. Almost all (92%,  $n = 440$ ) dispensed liquid formulations were available as a marketed solid form. Among them, 45% ( $n = 214$ ) were available in a solid form with a dosage exactly corresponding to the prescribed dose. When additionally considering acceptable dose rounding, a total of 80% ( $n = 379$ ) of prescribed liquid formulations could be substituted. Among those 379 acceptable solid dosage forms, 51% ( $n = 195$ ) would need to be divided to ensure dose acceptability, among which 56% ( $n = 109$ ) in halves



**Figure 1**

Flow chart of prescribed liquid formulation dispensed during 1 week by the BCH available in a suitable oral solid form for dosage and size

and 44% ( $n = 86$ ) in quarters. The proportion of solid dosage forms that would need division depending on the availability of exact prescribed dosage or adjusted prescribed dosage is detailed in Figure 1. Finally, also considering the size suitability of solid forms available in an acceptable dosage, the substitution rate was reduced to 41% (195/476).

The suitability of oral solid forms evaluated by children's age groups is presented in Table 1. Almost half (46%) of prescribed liquid drugs were intended for pre-school children (2 to 5 years old). The most widely prescribed liquid drugs were comparable among the three age groups. When considering only the dosage acceptabil-

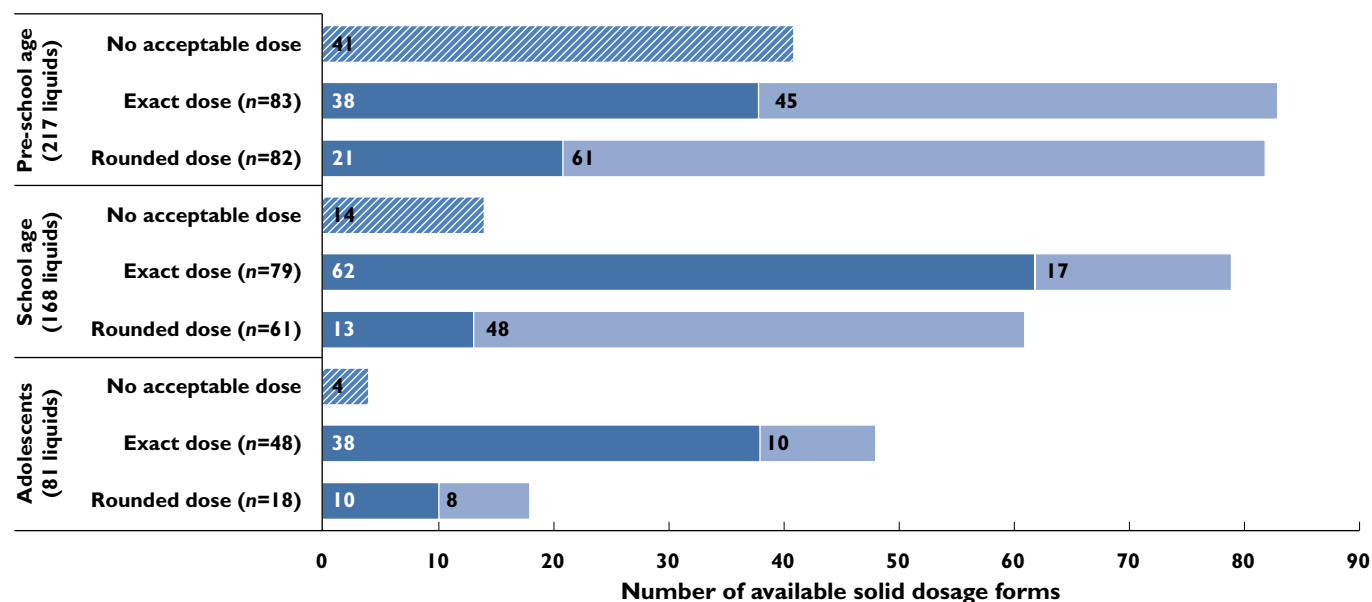
ity of available solid forms (including dose rounding), the substitution rate of liquid formulations with solid forms would be comparable between the three groups by age (76%, 83% and 81% respectively for pre-school children, school children and adolescents). In pre-school children, 64% (106/165) of acceptable solid dosage forms would require tablet division to achieve the prescribed dose exactly or after rounding the dose, with 61% halved and 39% quartered. The proportion of tablets that would need to be divided was of 46% in school children (65/140) and 27% in adolescents (18/66), with equal proportions of halved and quartered tablets for both age groups. The number of solid dosage forms that would require division

**Table 1**

Availability of oral solid forms depending on children's age groups

Age range*	Liquid formulations <i>n</i>	Available in an oral solid form		In an acceptable dosage†		In an acceptable size‡	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
All children	476	440	92.44	379	79.62	195	40.97
Pre-school children (2–5 years)	217	206	94.93	165	76.04	35	16.13
School children (6–11 years)	168	154	91.68	140	83.33	88	52.38
Adolescents (over 12 years)	81	70	86.42	66	81.48	64	79.01
Missing age data	10	10	–	8	–	8	–

\*Defined by the CHMP [2]. †Corresponding exactly to the prescribed dose or after adjustment of the prescribed dose. ‡Regarding children's age considering 2011 CHMP reflexion paper [23]. Percentages (%) correspond to the proportion of the total number of dispensed liquid formulations.

**Figure 2**

Distribution of available solid dosage forms for prescribed liquid drugs in the different children's age groups, depending on dosage acceptability and need for splitting tablets (hatched bar: no acceptable dose; solid blue bar: acceptable dose for whole tablet; solid blue bar: acceptable dose after splitting tablet)

depending on dosage suitability and children's age group is presented in Figure 2. When also considering the size suitability, the substitution rate becomes very low in the pre-school children (16.13%), who were considered unable to swallow tablets larger than 5 mm diameter, corresponding to commonly recognized mini-tablet size. The highest substitution rate of liquid formulations with solid forms, considering both dosage and size suitability, was identified for the adolescent group, with 79% of liquid formulations that could be substituted. Interestingly, in the school age group, 52% of prescribed liquid drugs could be converted to a solid form, which is an important finding to accommodate school life style. Finally, two thirds (152/249) of liquid formulations prescribed in children over 6

years could have been substituted with an oral solid form, suitable for both dose and size.

### Cost estimates

The substitution of liquid formulations with solid oral forms available in an acceptable dosage could result in a cost saving of £16K and £18K per week, respectively, for hospital and community sectors, corresponding to 73% and 76% of liquid formulation cost saved (Table 2). However, when additionally considering size suitability of available oral solid forms, these potential cost savings are reduced to £5K and £9K per week, respectively, for hospital and community (Table 3). Treatment costs of solid forms



**Table 2**

Costs of dispensed medicines during 1 week in the BCH, considering liquid formulations that could be substituted with a solid form acceptable for dosage ( $n = 379$ )

Age range*	Total cost of oral liquid medicines (£)		Total cost of oral solid form (£)		Potential cost saving (£)	
	Hospital	Community	Hospital	Community	Hospital	Community
All children	22 192	23 454	5 893	5 685	16 299	17 769
Pre-school children (2–5 years)	9 519	8 258	1 369	1 362	8 150	6 896
School children (6–11 years)	6 492	6 956	2 776	2 575	3 716	4 381
Adolescents (over 12 years)	6 035	7 398	1 724	1 724	4 311	5 673

\*Defined by the CHMP [2].

**Table 3**

Costs of dispensed medicines during 1 week in the BCH, considering liquid formulations that could be substituted with a solid form acceptable both for dosage and size ( $n = 195$ )

Age range*	Total cost of oral liquid medicines (£)		Total cost of oral solid form (£)		Potential cost saving (£)	
	Hospital	Community	Hospital	Community	Hospital	Community
All children	8 307	11 697	3 356	3 147	5 332	8 330
Pre-school children (2–5 years)	205	542	45	36	160	506
School children (6–11 years)	1 951	3 576	1 581	1 381	370	2 195
Adolescents (over 12 years)	6 018	7 348	1 216	1 719	4 802	5 629

\*Defined by the CHMP [2].

are nevertheless 50% less than treatment costs of liquid medicines.

## Discussion

Almost all dispensed oral liquid formulations in children over 2 years during 1 week in a paediatric hospital were available in a marketed solid oral form, and, more surprisingly, they had a dosage suitable for paediatric prescribing. The main limitation for liquid formulation substitution with solid form was the size of solid drugs, especially in children under 6 years of age. Despite this limitation, two-thirds of prescribed liquids could have been substituted with a suitable solid form for both dosage and size, with expected savings of around £5K and £8K in only 1 week, respectively, for hospital and community costs, corresponding to a projected annual saving of £238K and £410K, for only one study site.

These findings support numerous recent study results and expert opinion, which run contrary to the historic argument that liquid formulations are preferable for children. The main disadvantages associated with liquid formulations are related to their stability, potential toxicity, dosing and administration issues. The CHMP highlights the interest in using solid oral forms in young children with long term illness who require continuing medication. It

also recommends that, more generally, children be trained to swallow 'pills' from a relatively early age of 3–5 years [2]. In parallel, the WHO recommends that children of developing countries be treated with oral solid medicines for drugs that do not require a precise dose titration [6]. In addition, a small number of studies have provided evidence that the use of oral solid forms in children was associated with a greater acceptability and drug compliance than with liquid forms [15, 16, 18, 24, 25]. Spomer *et al.* have shown in an open randomized crossover study that, contrary to their original research hypothesis, mini-tablets (2 mm in diameter) acceptance in 60 children from 6 months to 6 years was at least equal or even better than that of sweet liquid, especially in very young children (0.5–1 years) [18]. Furthermore, complete refusal of oral administration was much higher for liquid than for solid formulation (40% of refusal vs. 10%). In a multicentre randomized study conducted by Van Riet-Nales *et al.* [24], 405 children from 1 to 4 years were selected to receive four oral placebo dosage forms: small tablet (4 mm), powder, suspension and syrup. The comparison of the dosage form acceptability showed that tablets were significantly better accepted than other forms ( $P < 0.001$ ). Interestingly, the number of fully swallowed administrations was also significantly higher with tablets ( $P < 0.05$ ). In Ansah *et al.*'s study, involving 301 children aged from 0 to 5 years, 91% of children who received pre-packed chloroquine tablets

complied with the prescribed treatment, compared with only 42% in children who received chloroquine syrup ( $P < 0.001$ ) [15]. The economic evaluation in the present study has shown that tablet treatment was five times less costly than current prescribed formulations. Increased patient (child) autonomy, a higher transportability, a single dose packaging and saving time for caregivers seems to be the most likely explanation for better drug compliance with solid oral forms in children [26, 27].

One of the limitations of our study was to base the size acceptability substitution on the 2011 edition of CHMP's Pharmaceutical Development of Medicines for Paediatric Use [26]. Although these recommendations were not based on evidence but on expert opinion and are now removed from the updated draft [3], given the lack of published evidence, they provide an insight into suitable solid size in children. In addition, CHMP note that tablet size acceptability may be improved using pill swallowing training and fractioning tablets, allowing very young children to swallow larger size solid forms [2]. Since the potential substitution rate of liquid formulations with solid forms when considering both dosage and size was sharply reduced, this point is of considerable importance. Indeed, the annual projected cost saving if we consider that children would be able to swallow all solid forms with an acceptable dose would be £782K and £853K, respectively, for hospital and community costs, or more than twice that if we also consider the pill size.

The suitability study of liquid drug substitution with solid forms was conducted considering the possibility of splitting tablets to achieve the prescribed dose. This methodological choice reflects a widespread clinical practice in our paediatric hospitals, where tablet splitters are made available when required. Indeed, breaking tablets is the most common oral dosage form manipulation, undertaken by caregivers for home carers or by nurses [28]. The magnitude of splitting tablet practice in paediatric wards has been poorly investigated. Fontan *et al.* have collected direct observations of nurse's administration habits in 14 French paediatric hospitals. The results revealed that around half (46.7%) of administered tablets were split before administration, most frequently by hand (55.3%) [29]. However, this study concerned young children ( $12.6 \pm 17$  months). Richey *et al.*'s multicentre study conducted in UK paediatric wards has shown that, among 40 observed tablet manipulations, 65% corresponded to splitting tablets, other practices being dispersing (30%) and crushing (2.5%) [30]. The high observed rates of splitting tablet practice in paediatric care compared with adults can easily be explained knowing that oral solid dosage forms are developed to meet the needs of adult patients [31]. From CHMP's reflexion paper on formulation of choice for the paediatric population, scoring tablets should be considered in paediatric care to improve solid form dosage flexibility and make tablets easier to swallow [2]. Although we considered such practice only for appro-

priate solid forms, coated and time-released tablets being excluded, consequences of solid form splitting on active drug efficacy and safety should, however, be assessed. Splitting tablets relies on the assumption that the active drug is uniformly distributed throughout the product. Nevertheless, several studies have shown that drug amount in tablet segments is often unequal, even using scored tablets. In addition, tablets can be difficult to cut, crumble and finally be inappropriately divided [30]. If tablet splitters seem to improve accuracy of division compared with hand or knife breaking, these devices also have significant segment inequality, in particular when tablets are small and quartered [32–34]. In our study, 23% of acceptable solid forms would need to be quartered. In addition, the need for splitting tablets was higher when the prescribed dose was rounded, adding further deviation from the initially prescribed dose. In practice, paediatricians and pharmacists should consider the need for tablet division, especially for small, unscored and low dosage tablets, prior to formulation choice. As regards children's ability to swallow, it is expected that splitting tablets will reduce palatability. Tablets when divided often have rough edges, may crumble and reveal the active drug taste [33]. However, Richey *et al.* report the case of a child who preferred split tablets to liquid, due to liquid bad taste and excess liquid volume to be swallowed [30]. Finally, from our results, dividing tablets offers interesting opportunities to adapt solid dosage forms for children and allows raising the rate of acceptable solid forms for dosage from 39% to 80%. This practice, however, has unknown consequences on active drug accuracy, drug stability and bioavailability [20, 30, 33]. Concern about dose deviations in children should focus on narrow therapeutic range drugs [35]. Among the 195 solid forms that would need to be split to achieve the prescribed dose, only one drug had a narrow therapeutic range (quartered gabapentin) in a 3-year-old child. Lastly, one of the major advantages of oral solid forms, which is that it is ready to use and offers easy dose selection, is reduced using this time-consuming practice. By the same reasoning, the impact of tablet splitting on drug adherence and administration error risks should also be assessed [30]. Splitting tablets, however, remains far preferable to crushing or dispersing tablets, involving greater risks for drug deterioration and administration error [20].

It might be seen as a limitation to conduct the cost study considering that all the split tablet's segments could be administered. Splitting tablets allows significant cost savings when each tablet section is administered, and could interestingly reduce treatment costs [31, 33]. Indeed, divided tablets would generally be less costly than the whole solid dosage form. In our own institution using all tablet sections is variable. Tablet splitters have a space to store unused tablet sections and are often provided for use at home, and the pharmacy can provide pre-split tablets if necessary, although this is rare. In the Fontan *et al.* study,

only half of divided tablet's segments were actually kept by nurses and administered [29]. To our knowledge, concerning home administration, no quantified data are available in the literature. When treatment cost is covered by health care insurance, the patient's main reasons for dividing tablets are to achieve the prescribed dose, ease swallowing and reduce dose, without economic considerations [36]. From our experience, we assume that patients with long term treatment are more inclined to keep tablet segments than patients with short term treatments. Finally, considering that every tablet's segment would be administered may have led to an overestimated cost saving associated with solid form use in children.

Some recent solid oral forms (e.g. powders, chewable, melt or oro-dispersible dosage forms) may provide another interesting alternative to liquid formulations in children, providing appropriate dosage and avoiding splitting tablets. However, few have been licensed for children under 4 years old, and must be provided 'off-label'. Furthermore, in spite of their practical advantages, they are much more costly than conventional solid drugs and, consequently, there are very few available on the market [1]. An evaluation of cost effectiveness regarding compliance improvement and comparing with conventional formulations is needed. More generally, the development of new paediatric medicines is complex, time consuming and costly. Insofar as cost may be a long term obstacle to widespread adoption of these new paediatric drug formulations, the immediate effective solution would be the use of already available alternatives, the most obvious being the solid oral form. Further work is required to identify the limits of oral solid forms use in paediatrics, in order to propose appropriate changes. From our results, the absolute necessity to facilitate solid oral form use in paediatrics is to reduce tablet size, making them more suitable for younger children and to facilitate swallowing learning for children. Developing solid dosage forms adapted to paediatric doses (e.g. mini-tablets) or securing splitting tablets (e.g. highly divisible tablets, scored tablets with drug-free basal compartment) would also help provide more suitable solid forms in children [37]. Awareness of pharmaceutical companies to this critical issue is an essential prerequisite for change. Community and paediatric hospital pharmacists should also consider the size parameter in drug selection. Another particularly attractive solution is the implementation of pill swallowing training in paediatric hospitals, in order to improve children's ability to swallow orally administered solids, especially for children with chronic illnesses requiring long term medication [38–46]. Numerous research teams have worked on this focus and methods for this behavioural change technique are now well defined. In Czyzewski *et al.*'s study, the largest capsule size was 19.4 mm, showing that pill swallowing training is effective even for large sized solid oral forms [38]. Given the cost savings that could be obtained when substituting liquid formulations with solid form in only 1

week in a single hospital, it is of major interest to evaluate the cost effectiveness of pill swallowing training implementation in a paediatric hospital for children who require long term medication. To conclude, expected practical and clinical advantages of oral solid form use in children have to be carefully considered against challenges related to children's ability to swallow and risks arising from splitting tablets. A larger long term multicentre study would help to investigate further solid forms suitability in children, consider the different therapeutic classes, treatment duration, required solid form manipulations and represent more accurately the diversity of prescribed drugs in paediatrics.

## Competing Interests

All authors have completed the Unified Competing Interest form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work or activities that could appear to have influenced the submitted work.

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